EXHIBIT 5

Medicare Benefit Policy Manual

Chapter 15 – Covered Medical and Other Health Services

Table of Contents

(Rev. 64, 01-19-07)
(Rev. 70, 05-11-07)
(Rev. 71, 05-25-07)
(Rev. 72, 05-25-07)

Transmittals for Chapter 15

Crosswalk to Old Manual

- They have not been determined by the FDA to be less than effective. (See §§50.4.4).

Medicare Part B does generally not cover drugs that can be self-administered, such as those in pill form, or are used for self-injection. However, the statute provides for the coverage of some self-administered drugs. Examples of self-administered drugs that are covered include blood-clotting factors, drugs used in immunosuppressive therapy, erythropoietin for dialysis patients, osteoporosis drugs for certain homebound patients, and certain oral cancer drugs. (See §110.3 for coverage of drugs, which are necessary to the effective use of Durable Medical Equipment (DME) or prosthetic devices.)

50.1 - Definition of Drug or Biological

(Rev. 1, 10-01-03)
B3-2049.1

Drugs and biologicals must be determined to meet the statutory definition. Under the statute §1861(t)(1), payment may be made for a drug or biological only where it is included, or approved for inclusion, in the latest official edition of the United States Pharmacopoeia National Formulary (USP-NF), the United States Pharmacopoeia-Drug Information (USD-DI), or the American Dental Association (AOA) Guide to Dental Therapeutics, except for those drugs and biologicals unfavorably evaluated in the ADA Guide to Dental Therapeutics. The inclusion of an item in the USP DI does not necessarily mean that the item is a drug or biological. The USP DI is a database of drug information developed by the U.S. Pharmacopoeia but maintained by Micromedex, which contains medically accepted uses for generic and brand name drug products. Inclusion in such reference (or approval by a hospital committee) is a necessary condition for a product to be considered a drug or biological under the Medicare program, however, it is not enough. Rather, the product must also meet all other program requirements to be determined to be a drug or biological. Combination drugs are also included in the definition of drugs if the combination itself or all of the therapeutic ingredients of the combination are included, or approved for inclusion, in any of the above drug compendia.

Drugs and biologicals are considered approved for inclusion in a compendium if approved under the established procedure by the professional organization responsible for revision of the compendium.

50.2 - Determining Self-Administration of Drug or Biological

(Rev. 1, 10-01-03)
AB-02-072, AB-02-139, B3-2049.2

The Medicare program provides limited benefits for outpatient prescription drugs. The program covers drugs that are furnished "incident to" a physician's service provided that the drugs are not usually self-administered by the patients who take them. Section 112 of the Benefits, Improvements & Protection Act of 2000 (BIPA) amended sections 1861(s)(2)(A) and 1861(s)(2)(B) of the Act to redefine this exclusion. The prior statutory

language referred to those drugs "which cannot be self-administered." Implementation of the BIPA provision requires interpretation of the phrase "not usually self-administered by the patient".

A. Policy

Fiscal intermediaries and carriers are instructed to follow the instructions below when applying the exclusion for drugs that are usually self-administered by the patient. Each individual contractor must make its own individual determination on each drug. Contractors must continue to apply the policy that not only the drug is medically reasonable and necessary for any individual claim, but also that the route of administration is medically reasonable and necessary. That is, if a drug is available in both oral and injectable forms, the injectable form of the drug must be medically reasonable and necessary as compared to using the oral form.

For certain injectable drugs, it will be apparent due to the nature of the condition(s) for which they are administered or the usual course of treatment for those conditions, they are, or are not, usually self-administered. For example, an injectable drug used to treat migraine headaches is usually self-administered. On the other hand, an injectable drug, administered at the same time as chemotherapy, used to treat anemia secondary to chemotherapy is not usually self-administered.

B. Administered

The term "administered" refers only to the physical process by which the drug enters the patient's body. It does not refer to whether the process is supervised by a medical professional (for example, to observe proper technique or side-effects of the drug). Only injectable (including intravenous) drugs are eligible for inclusion under the "incident to" benefit. Other routes of administration including, but not limited to, oral drugs, suppositories, topical medications are all considered to be usually self-administered by the patient.

C. Usually

For the purposes of applying this exclusion, the term "usually" means more than 50 percent of the time for all Medicare beneficiaries who use the drug. Therefore, if a drug is self-administered by more than 50 percent of Medicare beneficiaries, the drug is excluded from coverage and the contractor may not make any Medicare payment for it. In arriving at a single determination as to whether a drug is usually self-administered, contractors should make a separate determination for each indication for a drug as to whether that drug is usually self-administered.

After determining whether a drug is usually self-administered for each indication, contractors should determine the relative contribution of each indication to total use of the drug (i.e., weighted average) in order to make an overall determination as to whether the drug is usually self-administered. For example, if a drug has three indications, is not

self-administered for the first indication, but is self administered for the second and third indications, and the first indication makes up 40 percent of total usage, the second indication makes up 30 percent of total usage, and the third indication makes up 30 percent of total usage, then the drug would be considered usually self-administered.

Reliable statistical information on the extent of self-administration by the patient may not always be available. Consequently, CMS offers the following guidance for each contractor's consideration in making this determination in the absence of such data:

1. Absent evidence to the contrary, presume that drugs delivered intravenously are not usually self-administered by the patient.

2. Absent evidence to the contrary, presume that drugs delivered by intramuscular injection are not usually self-administered by the patient. (Avonex, for example, is delivered by intramuscular injection, not usually self-administered by the patient.) The contractor may consider the depth and nature of the particular intramuscular injection in applying this presumption. In applying this presumption, contractors should examine the use of the particular drug and consider the following factors:

3. Absent evidence to the contrary, presume that drugs delivered by subcutaneous injection are self-administered by the patient. However, contractors should examine the use of the particular drug and consider the following factors:

    A. **Acute Condition -** Is the condition for which the drug is used an acute condition? If so, it is less likely that a patient would self-administer the drug. If the condition were longer term, it would be more likely that the patient would self-administer the drug.

    B. **Frequency of Administration -** How often is the injection given? For example, if the drug is administered once per month, it is less likely to be self-administered by the patient. However, if it is administered once or more per week, it is likely that the drug is self-administered by the patient.

In some instances, carriers may have provided payment for one or perhaps several doses of a drug that would otherwise not be paid for because the drug is usually self-administered. Carriers may have exercised this discretion for limited coverage, for example, during a brief time when the patient is being trained under the supervision of a physician in the proper technique for self-administration. Medicare will no longer pay for such doses. In addition, contractors may no longer pay for any drug when it is administered on an outpatient emergency basis, if the drug is excluded because it is usually self-administered by the patient.

D. Definition of Acute Condition

For the purposes of determining whether a drug is usually self-administered, an acute condition means a condition that begins over a short time period, is likely to be of short duration and/or the expected course of treatment is for a short, finite interval. A course of treatment consisting of scheduled injections lasting less than two weeks, regardless of frequency or route of administration, is considered acute. Evidence to support this may include Food and Drug administration (FDA) approval language, package inserts, drug compendia, and other information.

E. By the Patient

The term "by the patient" means Medicare beneficiaries as a collective whole. The carrier includes only the patients themselves and not other individuals (that is, spouses, friends, or other care-givers are not considered the patient). The determination is based on whether the drug is self-administered by the patient a majority of the time that the drug is used on an outpatient basis by Medicare beneficiaries for medically necessary indications. The carrier ignores all instances when the drug is administered on an inpatient basis.

The carrier makes this determination on a drug-by-drug basis, not on a beneficiary-by-beneficiary basis. In evaluating whether beneficiaries as a collective whole self-administer, individual beneficiaries who do not have the capacity to self-administer any drug due to a condition other than the condition for which they are taking the drug in question are not considered. For example, an individual afflicted with paraplegia or advanced dementia would not have the capacity to self-administer any injectable drug, so such individuals would not be included in the population upon which the determination for self-administration by the patient was based. Note that some individuals afflicted with a less severe stage of an otherwise debilitating condition would be included in the population upon which the determination for "self-administered by the patient" was based; for example, an early onset of dementia.

F. Evidentiary Criteria

Contractors are only required to consider the following types of evidence: peer reviewed medical literature, standards of medical practice, evidence-based practice guidelines, FDA approved label, and package inserts. Contractors may also consider other evidence submitted by interested individuals or groups subject to their judgment.

Contractors should also use these evidentiary criteria when reviewing requests for making a determination as to whether a drug is usually self-administered, and requests for reconsideration of a pending or published determination.

Please note that prior to the August 1, 2002, one of the principal factors used to determine whether a drug was subject to the self-administered exclusion was whether the FDA label contained instructions for self-administration. However, CMS notes that under the new standard, the fact that the FDA label includes instructions for self-administration is not, by itself, a determining factor that a drug is subject to this exclusion.

G. Provider Notice of Noncovered Drugs

Contractors must describe on their Web site the process they will use to determine whether a drug is usually self-administered and thus does not meet the "incident to" benefit category. Contractors must publish a list of the injectable drugs that are subject to the self-administered exclusion on their Web site, including the data and rationale that led to the determination. Contractors will report the workload associated with developing new coverage statements in CAFM 21208.

Contractors must provide notice 45 days prior to the date that these drugs will not be covered. During the 45-day time period, contractors will maintain existing medical review and payment procedures. After the 45-day notice, contractors may deny payment for the drugs subject to the notice.

Contractors must not develop local medical review policies (LMRPs) for this purpose because further elaboration to describe drugs that do not meet the 'incident to' and the 'not usually self-administered' provisions of the statute are unnecessary. Current LMRPs based solely on these provisions must be withdrawn. LMRPs that address the self-administered exclusion and other information may be reissued absent the self-administered drug exclusion material. Contractors will report this workload in CAFM 21206. However, contractors may continue to use and write LMRPs to describe reasonable and necessary uses of drugs that are not usually self-administered.

H. Conferences Between Contractors

Contractors' Medical Directors may meet and discuss whether a drug is usually self-administered without reaching a formal consensus. Each contractor uses its discretion as to whether or not it will participate in such discussions. Each contractor must make its own individual determinations, except that fiscal intermediaries may, at their discretion, follow the determinations of the local carrier with respect to the self-administered exclusion.

I. Beneficiary Appeals

If a beneficiary's claim for a particular drug is denied because the drug is subject to the "self-administered drug" exclusion, the beneficiary may appeal the denial. Because it is a "benefit category" denial and not a denial based on medical necessity, an Advance Beneficiary Notice (ABN) is not required. A "benefit category" denial (i.e., a denial based on the fact that there is no benefit category under which the drug may be covered) does not trigger the financial liability protection provisions of Limitation On Liability (under §1879 of the Act). Therefore, physicians or providers may charge the beneficiary for an excluded drug.

J. Provider and Physician Appeals

A physician accepting assignment may appeal a denial under the provisions found in Chapter 29 of the Medicare Claims Processing Manual.

K. Reasonable and Necessary

Carriers and fiscal intermediaries will make the determination of reasonable and necessary with respect to the medical appropriateness of a drug to treat the patient's condition. Contractors will continue to make the determination of whether the intravenous or injection form of a drug is appropriate as opposed to the oral form. Contractors will also continue to make the determination as to whether a physician's office visit was reasonable and necessary. However, contractors should not make a determination of whether it was reasonable and necessary for the patient to choose to have his or her drug administered in the physician's office or outpatient hospital setting. That is, while a physician's office visit may not be reasonable and necessary in a specific situation, in such a case an injection service would be payable.

L. Reporting Requirements

Each carrier and intermediary must report to CMS, every September 1 and March 1, its complete list of injectable drugs that the contractor has determined are excluded when furnished incident to a physician's service on the basis that the drug is usually self-administered. The CMS anticipates that contractors will review injectable drugs on a rolling basis and publish their list of excluded drugs as it is developed. For example, contractors should not wait to publish this list until every drug has been reviewed. Contractors must send their exclusion list to the following e-mail address: drugdata@cms.hhs.gov a template that CMS will provide separately, consisting of the following data elements in order:

1. Carrier Name
2. State
3. Carrier ID#
4. HCPCS
5. Descriptor
6. Effective Date of Exclusion
7. End Date of Exclusion
8. Comments

Any exclusion list not provided in the CMS mandated format will be returned for correction.

To view the presently mandated CMS format for this report, open the file located at: http://cms.hhs.gov/manuals/pm_trans/AB02_139a.zip

50.3 - Incident-to Requirements

(Rev. 1, 10-01-03)

B3-2049.3

In order to meet all the general requirements for coverage under the incident-to provision, an FDA approved drug or biological must:

- Be of a form that is not usually self-administered;
- Must be furnished by a physician; and
- Must be administered by the physician, or by auxiliary personnel employed by the physician and under the physician's personal supervision.

The charge, if any, for the drug or biological must be included in the physician's bill, and the cost of the drug or biological must represent an expense to the physician. Drugs and biologicals furnished by other health professionals may also meet these requirements. (See §§170, 180, 190 and 200 for specific instructions.)

Whole blood is a biological, which cannot be self-administered and is covered when furnished incident to a physician's services. Payment may also be made for blood fractions if all coverage requirements are satisfied and the blood deductible has been met.

50.4 - Reasonableness and Necessity

(Rev. 1, 10-01-03)
B3-2049.4

50.4.1 - Approved Use of Drug

(Rev. 1, 10-01-03)
B3-2049.4

Use of the drug or biological must be safe and effective and otherwise reasonable and necessary. (See the Medicare Benefit Policy Manual, Chapter 16, "General Exclusions from Coverage," §20.) Drugs or biologicals approved for marketing by the Food and Drug Administration (FDA) are considered safe and effective for purposes of this requirement when used for indications specified on the labeling. Therefore, the program may pay for the use of an FDA approved drug or biological, if:

- It was injected on or after the date of the FDA's approval;
- It is reasonable and necessary for the individual patient; and
- All other applicable coverage requirements are met.

The carrier, DMERC, or intermediary will deny coverage for drugs and biologicals, which have not received final marketing approval by the FDA unless it receives instructions from CMS to the contrary. For specific guidelines on coverage of Group C cancer drugs, see the Medicare National Coverage Determinations Manual.

If there is reason to question whether the FDA has approved a drug or biological for marketing, the carrier or intermediary must obtain satisfactory evidence of FDA's approval. Acceptable evidence includes:

- A copy of the FDA's letter to the drug's manufacturer approving the new drug application (NDA);
- A listing of the drug or biological in the FDA's "Approved Drug Products" or "FDA Drug and Device Product Approvals";
- A copy of the manufacturer's package insert, approved by the FDA as part of the labeling of the drug, containing its recommended uses and dosage, as well as possible adverse reactions and recommended precautions in using it; or
- Information from the FDA's Web site.

When necessary, the regional office (RO) may be able to help in obtaining information.

50.4.2 - Unlabeled Use of Drug

(Rev. 1, 10-01-03)
B3-2049.3

An unlabeled use of a drug is a use that is not included as an indication on the drug's label as approved by the FDA. FDA approved drugs used for indications other than what is indicated on the official label may be covered under Medicare if the carrier determines the use to be medically accepted, taking into consideration the major drug compendia, authoritative medical literature and/or accepted standards of medical practice. In the case of drugs used in an anti-cancer chemotherapeutic regimen, unlabeled uses are covered for a medically accepted indication as defined in §50.5.

These decisions are made by the contractor on a case-by-case basis.

50.4.3 - Examples of Not Reasonable and Necessary

(Rev. 1, 10-01-03)
B3-2049.4

Determinations as to whether medication is reasonable and necessary for an individual patient should be made on the same basis as all other such determinations (i.e., with the advice of medical consultants and with reference to accepted standards of medical practice and the medical circumstances of the individual case). The following guidelines identify three categories with specific examples of situations in which medications would not be reasonable and necessary according to accepted standards of medical practice:

1. Not for Particular Illness

Medications given for a purpose other than the treatment of a particular condition, illness, or injury are not covered (except for certain immunizations). Charges for medications, e.g., vitamins, given simply for the general good and welfare of the patient and not as accepted therapies for a particular illness are excluded from coverage.

2. Injection Method Not Indicated

Medication given by injection (parenterally) is not covered if standard medical practice indicates that the administration of the medication by mouth (orally) is effective and is an accepted or preferred method of administration. For example, the accepted standard of medical practice for the treatment of certain diseases is to initiate therapy with parenteral penicillin and to complete therapy with oral penicillin. Carriers exclude the entire charge for penicillin injections given after the initiation of therapy if oral penicillin is indicated unless there are special medical circumstances that justify additional injections.

3. Excessive Medications

Medications administered for treatment of a disease and which exceed the frequency or duration of injections indicated by accepted standards of medical practice are not covered. For example, the accepted standard of medical practice in the maintenance treatment of pernicious anemia is one vitamin B-12 injection per month. Carriers exclude the entire charge for injections given in excess of this frequency unless there are special medical circumstances that justify additional injections.

Carriers will supplement the guidelines as necessary with guidelines concerning appropriate use of specific injections in other situations. They will use the guidelines to screen out questionable cases for special review, further development, or denial when the injection billed for would not be reasonable and necessary. They will coordinate any type of drug treatment review with the Quality Improvement Organization (QIO).

If a medication is determined not to be reasonable and necessary for diagnosis or treatment of an illness or injury according to these guidelines, the carrier excludes the entire charge (i.e., for both the drug and its administration). Also, carriers exclude from payment any charges for other services (such as office visits) which were primarily for the purpose of administering a noncovered injection (i.e., an injection that is not reasonable and necessary for the diagnosis or treatment of an illness or injury).

50.4.4 - Payment for Antigens and Immunizations
(Rev. 1, 10-01-03)

50.4.4.1 - Antigens
(Rev. 1, 10-01-03)
B3-2049.4

Payment may be made for a reasonable supply of antigens that have been prepared for a particular patient if: (1) the antigens are prepared by a physician who is a doctor of